



FEB. 17, 2005

HEALTH UPDATE

**“Impact of Influenza Vaccination on Seasonal Mortality in the US
Elderly Population” by Simonsen et al. (2005)
Points and Q&As
(2/15/05)**

Key Messages

- **CDC continues to recommend that people aged 65 and older get vaccinated against influenza each year.**
- Persons aged 65 and older are at high risk for complications, hospitalizations, and deaths from influenza.
- Vaccination is the best way for people 65 and older to protect themselves (and their loved ones) from influenza.

The Study:

- **The Simonsen et al. study does not show that the flu vaccine is ineffective at protecting the elderly from influenza.** Rather, the study indicates that different research approaches result in different estimates of influenza vaccine effectiveness at preventing death among the elderly.
- **The Simonsen study has some significant limitations when it comes to assessing the effectiveness of influenza vaccination.**
 - The study analyzes patterns of influenza vaccination and death among the elderly from 1961 to 2001 and suggests a relationship between the two. This type of analysis is called an “ecologic study”.
 - Ecologic studies look at overall trends and don’t include information on specific individuals, such as vaccination status and health conditions.
 - Since there is no information on which of the individuals who died were vaccinated or their underlying conditions, the death and vaccination patterns identified in this study cannot be directly linked. Apparent associations can be inferred, but may be misleading or hard to interpret.
- **Many previously published "observational studies" suggest a higher level of influenza vaccine effectiveness against death in the elderly than indicated in the Simonsen paper.**

- There are several types of epidemiologic studies, including ecologic studies, observational studies (e.g., studies that compare vaccinated people to people who choose not to get vaccinated), and clinical trials (or experiments), where people are randomly assigned to a treatment or control group. Clinical trials provide the most reliable and valid data on vaccine effectiveness. However, conducting a true clinical trial of the effect of influenza vaccine in the elderly would be unethical, because investigators would randomly assign participants to get vaccine or not, despite the fact that influenza vaccination has been recommended for many years for all those aged 65 and older. So, to study vaccine effectiveness researchers have observed what has happened among people who have chosen on their own to be vaccinated and those who have not (called “observational studies”).
- Observational studies to date have generally found that when the "match" between the vaccine and circulating influenza strains is close, the vaccine is 30%-70% effective in preventing hospitalization for pneumonia and influenza among elderly persons living outside chronic-care facilities (such as nursing homes) and those persons with long-term (chronic) medical conditions. Observational studies have also found that among elderly nursing home residents, the flu shot can be 50%-60% effective in preventing hospitalization or pneumonia and up to 80% effective in preventing death from the flu.
- The main weakness of observational studies is that they are likely to be influenced by selection bias (e.g., if very vulnerable elderly people are less likely to get vaccinated than the relatively healthy elderly, then this bias might lead to overestimates of vaccine effectiveness for preventing deaths).
- The main strength of observational studies is that information on individuals is analyzed and factors that may bias the result can be taken into account during the analysis. For this reason, observational studies have been considered more appropriate than ecologic studies for evaluating vaccine effectiveness.
- **The Department of Health and Human Services and CDC have both recognized that more needs to be done to protect people aged 65 and over from influenza, and efforts are under way to do so:**
 - Additional studies could be helpful to establish the effectiveness of the vaccine in preventing influenza complications and deaths.
 - CDC recognizes that influenza vaccine provides less-than-optimal protection against flu for people aged 65 and older and that additional steps should be taken to help protect them.
 - Such steps include improving vaccination coverage (including among people with frequent and close contact with the elderly so infection is passed to them less often), moving toward "universal" immunization as the vaccine supply allows, developing influenza vaccines that are more effective in people age 65 and over, and effectively using influenza antiviral drugs.

Questions and Answers

How do you explain the apparent contradiction between the results obtained by Simonsen et al and the results obtained by previously published studies?

Neither previous studies nor the Simonsen paper have all the information needed to determine influenza vaccine effectiveness in preventing death among people aged 65 and older. It is possible that both types of studies (i.e., ecologic and observational) might be partly right but capture the picture incompletely. While studies indicate that the vaccine is not as effective in persons aged 65 and older as we would like it to be, vaccination remains the best way to protect this population against complications, hospitalization, and death from influenza.

Did previous studies overstate the effectiveness of influenza immunization at preventing deaths in the elderly?

Many previously published "observational studies" suggest a higher level of influenza vaccine effectiveness against death in the elderly than indicated in the Simonsen paper. The main strength of these studies is that they include information about individuals (e.g., whether they were vaccinated or not, and if they have chronic medical conditions). However, all observational studies can be affected by certain "biases", so it is possible that they overestimated the vaccine's effectiveness at preventing death in the elderly (just as it is possible that the Simonsen study underestimates the vaccine's effectiveness). For example, if very vulnerable people are less likely to get vaccinated than the relatively healthy elderly, then this bias can affect calculated vaccine effectiveness estimates. In this instance, one would guess that this bias would lead to overestimates of vaccine effectiveness for preventing deaths. Although the Simonsen article suggests that the previously published observational studies overestimate the vaccine's effectiveness, it is possible that both types of studies might be partly right but capture the picture incompletely.

Do these findings mean that the vaccine does not work for people aged 65 and over?

No, the findings do not mean that the vaccine is not effective in protecting people age 65 and over from influenza complications, hospitalization, and death.

- Most importantly, since there is no information on which of the individuals who died were vaccinated or their underlying conditions, the death and vaccination patterns identified in this study cannot be directly linked. Apparent associations can be inferred, but may be misleading or hard to interpret.
- The authors looked only at mortality (i.e., death), not hospitalizations or other severe outcomes associated with influenza.
- The study also lacked the statistical power to rule out a modest reduction in influenza-related mortality during 1980-2001 that would correspond to the vaccine being up to half as effective in the elderly as it is in younger people.

Are there other explanations for the trends identified in this paper?

The authors suggest that because influenza vaccine coverage is increasing in the elderly over a period during which age-specific mortality rates have not decreased that the vaccine must be ineffective. Yet because the authors have no information regarding health status, it is equally as likely that the prevalence of high-risk conditions increased in the elderly during the years the study was conducted. These are among the reasons why the CDC has never made assessments of vaccine effectiveness or safety using ecologic study designs.

In addition, the authors do not use virological data -- by far the most reliable measure -- to define the length of influenza seasons during the study period. They suggest seasons grew shorter but in fact, reliable national viral surveillance data indicate the opposite. This fact could influence the trends of influenza-attributable deaths over time and affect results obtained in this paper.

What are the strengths of the Simonsen study?

In general, the elderly have immune systems that are less able to fight new infections; because of declining immunity, they also may not respond as well to the influenza vaccine. The study by Simonsen and colleagues emphasizes the particular vulnerability of this group and the need to develop other approaches in addition to direct vaccination for protecting them against influenza.

What are the limitations of the Simonsen study?

The primary limitation of the Simonsen analysis is that, as an "ecologic study", it analyzes patterns of death and vaccination among the elderly and suggests a relationship between the two. Since there is no information on which of the individuals who died were vaccinated or their underlying conditions, the death and vaccination patterns identified in this study cannot be directly linked. Apparent associations can be inferred, but may be misleading.

The authors suggest that the vaccine would have prevented few deaths among people 65-74 years of age because they already had immunity from previous exposure to flu viruses in their youth? If this is the case, why bother vaccinating them?

There are little data to support the contention that few deaths from influenza could have been prevented among those aged 65-74 years, due to previous exposure to A(H3N2) viruses in their youth.

What is being done to better protect people aged 65 and older from influenza?

The Department of Health and Human Services has recognized that more needs to be done to protect people aged 65 and over from influenza and efforts are under way to do so. Such steps include improving vaccination coverage, moving toward "universal" immunization as the supply allows, developing influenza vaccines that are more effective in people aged 65 and over, and effectively using influenza antiviral drugs.

Will CDC change influenza immunization recommendations for people aged 65 and over based on the findings in this study?

No. CDC will continue to recommend vaccination of people aged 65 and over to protect them from influenza. In setting immunization recommendations, CDC (in coordination with the Advisory Committee on Immunization Practices) considers the body of scientific evidence regarding a vaccine's efficacy and safety, as well as the public health impact of the disease the vaccine prevents. Many previously published "observational studies" suggest a higher level of influenza vaccine effectiveness against death in the elderly than indicated in the Simonsen paper. In light of the larger body of evidence, and in light of the risks posed to the elderly by influenza, CDC will not change influenza immunization recommendations for people aged 65 and over.

Categories of Health Alert messages:

- *Health Alert conveys the highest level of importance; warrants immediate action or attention.*
- *Health Advisory provides important information for a specific incident or situation; may not require immediate action.*
- *Health Update provides updated information regarding an incident or situation; no immediate action necessary.*
- *Health Information provides general information that is not necessarily considered to be of an emergent nature.*

This message is being sent to local public health units, clinics, hospitals, physicians, tribal health, North Dakota Nurses Association, North Dakota Long Term Care Association, North Dakota Healthcare Association, North Dakota Medical Association, and hospital public information officers.